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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,870	07/31/2003	Joel Myerson	10004042-2	4637

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EXAMINER	
LIU, SUE XU	
ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,870	MYERSON, JOEL	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/30/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-46* is/are pending in the application.

4a) Of the above claim(s) *41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-40, and 42-46* is/are rejected.

7)☒ Claim(s) *28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/31/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-26 have been cancelled as filed on 7/31/03;

Claims 27-46 are currently pending.

Claim 41 has been withdrawn.

Claims 27-40, and 42-46 are being examined in this application.

Election/Restrictions

1. Applicants elected the following species:

A.) Antibody or binding domain thereof as the "capture agent".

B.) Lysine as the "particular amino acid".

C.) A fluorescent tagged molecule as the labeling agent.

D.) Protein as the "target molecule".

in the reply filed on 10/30/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Consequently, the non-elected species are withdrawn from the corresponding claims, and Claim 41 has been withdrawn due to non-elected species.

Priority

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/773,886, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The instant application claims "an array of polypeptide capture agents", wherein the polypeptide capture agents are free of a particular amino acid. The instant claims further recite that the "particular amino acid is chosen from arginine, lysine, cysteine, histidine, aspartic acid or glutamic acid". Neither the specification nor the claims of the '886 application disclose polypeptides that are free of those particular amino acids except "lysine". The instant claims further recite that the "polypeptide capture agents" are made up of amino acids chosen from: ala, cys, asp..." (see Claim 35). Neither the specification nor the claims of the '886 application disclose polypeptides that are "made up" of these specific amino acid residues.

Thus, the effective filing date for the instant claimed subject matter that are not supported by the parent application is 7/31/2003.

Claim Objections

3. Claim 28 is objected to because of the following informalities: The claim as written is missing a "period". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

5. Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 35 has been added as part of a preliminary amendment filed on 7/31/03. However, the instant specification does not provide support for the claimed array recited in Claim 35. In particular, the instant specification and claims as originally filed do not disclose arrays of polypeptide capture agents that are "made up of" the specific amino acid residues listed in Claim 35.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claim 35 represents new matter.

Written Description Rejection

6. Claims 27-40, and 42-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite an array of polypeptide capture agents, wherein said polypeptide capture agents are linked to a substrate and are free of a particular amino acid. Applicant has selected antibodies and antibody fragments as the capture agents, Lysine as the particular amino acid, and protein as the target molecule.

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority.

The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

Claims 27-34, 36-40, and 42-46 are drawn to a genus of "polypeptide capture agents" that comprise various amino acid residues. The claims are basically drawn to any agents such as any antibodies with any amino acid sequences that do not have lysine residues. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of "polypeptide capture agents" (i.e. antibodies free of a particular amino acid such as lysine). In addition, no representative numbers of species for the claimed genus is provided to show possession of the claimed genus of antibodies that are free of lysine residues.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. (see MPEP 2163 II).

In this case, the instant application did not provide any limiting structure and/or functional characteristics for the claimed genus of antibodies without lysine residues. The instant specification is prophetic and does not provide any examples of specific "capture agent" that is an antibody without any lysine residues. The examples (p. 9+ of the instant spec.) listed in the instant specification only provide general discussion of generating proteins with mutations, but no examples of specific capture agent is described.

The state of the art at the time the invention was filed also does not teach every possible antibodies that possess no lysine residues. However, it is known in the art that antibodies have conserved lysine residues in different regions of antibody proteins, and the lysine residues may also be required for antigen (target protein) binding of the antibodies. For example, Attanasio et

al (Immunogenetics. Vol. 54: 556-561. 2002) review antibodies, and teaches that antibody chains from different organisms share conservative sequences that include "lysine" (K) residues (see p. 558 of Attanasio). Thommesen et al (Molecular Immunology. Vol. 37: 995-1004. 2000), teach a Lysine residue is crucial for antibody interactions (see Abstract of the reference). Thus, it is not known in the art that any antibody can be stably and functionally generated without any lysine residue in its amino acid sequence.

Furthermore, the instant specification also recites that "in the absence of lysine, more extensive modifications may need to be performed in order to maintain the desired properties of the non-variable scaffold region" (p. 10, lines 19+ of the spec.), which indicates that it is an essentially a trial and error process to generate antibodies without any lysine residues that can have the desired target binding properties.

Therefore, applicants are not in possession of the genus of capture agents that are antibodies without any lysine residues. Applicant's claimed scope represents only an invitation to experiment regarding possible antibodies that might be generated without lysine residues that can bind to protein targets.

Scope of Enablement Rejection

7. Claims 27-40, and 42-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain antibodies or fragments thereof without any lysine residues as capture agents for proteins, does not reasonably provide enablement for any antibodies that have no lysine residues. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described *In re Wands*, 8 USPQ2d 1400(1988). They are:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The predictability or lack thereof in the art
5. The level of skill in the art;
6. The amount of direction or guidance present;
7. The presence or absence of working examples;
8. The quantity of experimentation needed.

The breadth of the claims

The breadth of the claims seems to encompass a genus of "polypeptide capture agents" that comprise various amino acid residues. The claims are basically drawn to any agents such as any antibodies with any amino acid sequences that do not have lysine residues. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of "polypeptide capture agents" (i.e. antibodies free of a particular amino acid such as lysine). In addition, no representative numbers of species for the claimed genus is provided to show possession of the claimed genus of antibodies that are free of lysine residues.

The nature of the invention

The nature of the invention is array of polypeptide capture agents (antibodies) that are free of a particular amino acid (lysine).

The state of the prior art/ The predictability or lack thereof in the art

The state of the art at the time the invention was filed also does not teach every possible antibodies that possess no lysine residues. However, it is known in the art that antibodies have conserved lysine residues in different regions of antibody proteins, and the lysine residues may also be required for antigen (target protein) binding of the antibodies. For example, Attanasio reviews antibodies, and teaches that antibody chains from different organisms share conservative sequences that include "lysine" (K) residues (see p. 558 of Attanasio). Thommesen et al, teach a Lysine residue is crucial for antibody interactions (see Abstract of the reference). Thus, it is not known in the art that any antibody can be stably and functionally generated without any lysine residue in its amino acid sequence.

Furthermore, the instant specification also recites that "in the absence of lysine, more extensive modifications may need to be performed in order to maintain the desired properties of the non-variable scaffold region" (p. 10, lines 19+ of the spec.), which indicates that it is an essentially a trial and error process to generate antibodies without any lysine residues that can have the desired target binding properties.

The above discussion illustrates that the nature of the art (generating antibodies that are entirely free of a certain amino acid) is highly unpredictable. Although there may be suggested methods of overcoming these problems through non-routine experimentations, there are no

predictable methods or solutions that would solve all the problems for any antibodies that bind to any target proteins.

The level of one of ordinary skill

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction or guidance present/The presence or absence of working examples

The instant specification is prophetic and does not provide any examples of specific "capture agent" that is an antibody without any lysine residues. The examples (p. 9+ of the instant spec.) listed in the instant specification only provide general discussion of generating proteins with mutations, but no examples of specific capture agent is described.

The quantity of experimentation needed

Due to the unpredictabilities of generating antibodies that are entirely without certain amino acid, undue experimentation would be required. The art has not demonstrated all the possible antibodies that are without certain amino acid, and are capable of binding to desired protein targets. Because the instant specification does not provide specific guidance and/or examples for stable and functional antibodies that are entirely without lysine or other amino acid residues, undue experimentation would be required to use and/or make the claimed product of an array of capture agents.

Conclusion

Due to the non-routine experimentation necessary to determine the feasibility of generating antibodies that are devoid of lysine or other amino acids; the lack of direction/guidance presented in the specification regarding the specific structure and/or functional characteristic of the claimed capture agents; the unpredictability of making the antibodies; the breadth of the claims, undue experimentation would be required of a skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 29, 35-40, and 42-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 recites "wherein said particular amino acid is non-reactive with a labeling agent". However, Claim 27 from which claim 29 depends on recites that the claimed capture agents are "free of a particular amino acid". That is the claimed product of the independent claim 27 does not contain or comprise the "particular amino acid". However, Claim 29 seems to recite that the "particular amino acid" is contained within the capture agent and are non-reactive with a labeling agent.

Claim 35 recites "an array of polypeptide capture agents" are "made up of amino acids chosen from…", which is indefinite. It is not clear from the said claim which amino acids are

contained within the polypeptide capture agents. It is also not clear if the polypeptide capture agents consist only of those listed amino acids or additional amino acids are permitted. The instant specification also does not define the amino acid residues that are comprised by the claimed "capture agents".

Claim 36 recites the limitation "the presence of a target polypeptide". There is insufficient antecedent basis for this limitation in the claim.

Claim 44 and its dependent claims (45 and 46) are indefinite, because they are ultimately dependent on a canceled claim (Claim 1).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

11. Claims 27, 29-40 and 42-46 are rejected under **35 U.S.C. 102(b)** as being anticipated by Fodor et al (US 5,424,186; 06/13/1995).

The instant claims recite an array of polypeptide capture agents, wherein said polypeptide capture agents are linked to a substrate and are free of a particular amino acid. Applicant has selected antibodies and antibody fragments as the capture agents, Lysine as the particular amino acid, and protein as the target molecule.

Fodor et al, throughout the patent, teach generating arrays with various polymers such as polynucleotides and polypeptides (Abstract and Col. 1+, and Figures), which the synthesized polypeptides on substrates reads on the array of "capture agents" of **clms 27, 36 and 44**. The reference also teaches the specific amino acid sequences for the peptides or polypeptides (see Figures, col. 26+, cols. 45+), which reads on the different capture agents free of lysine (col. 45, lines 60+) of **clms 27, 28, 30-36, 38,** and **39**. The polypeptide taught by Fodor et al also read on antibody or antibody fragments. For example, SEQ ID No 8 of Fodor et al match a fragment of an antibody such as SEQ ID No. 16 of Pope et al (US 5,977,319; 11/2/1999).

Because the "particular amino acid", lysine recited in the specification is structurally the same as the amino acid "lysine" known in the art (e.g. p. 10 of the spec.), and the instant specification has not demonstrated any distinguishing characteristics that would render the claimed "particular amino acid" structurally different from the ones known in the art and the Fodor reference, it is an inherent property for the "particular amino acid" to be non-reactive with a labeling agent as recited in **clm 29**.

The reference also teaches labeling the target proteins with fluorescently labeled antibodies (col. 25, lines 20+), which read on the target of **clm 42**, and the fluorescent label of **clms 36, 40, 43, 45,** and **46** because the "second receptor" (or antibody) only specifically binds to the "first receptor" and does not bind to the protein on the substrate.

The reference also teaches other fluorescent labels (col. 31-32; col.32, lines 5+), which reads on the labeling agent covalently bonds to a reactive side chain of the particular amino acid of **clm 37**.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 27-36, 38-40 and 42-46 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fodor et al (US 5,424,186; 06/13/1995).

Fodor et al, throughout the patent, teach arrays with various polymers such as polynucleotides and polypeptides, as discussed above.

Fodor et al, do not explicitly teach the "polypeptide captures agents are chemically modified so that they are free of said particular amino acid", as recited in **clm 28**.

However, the said phrase of the instant claim 28 is a product by process recitation.

Process steps per se cannot serve to limit the product claims. See In re Stephens, 345 F.2d 1020, 1023, 145 USPQ 656, 658 (CCPA 1965) ("We think it well settled that the presence of process limitations in product claims, which product does not otherwise patentably distinguish over the prior art, cannot impart patentability to that product."). The relevant inquiry in a product-by-process claim is how the process recitations might define structure. See, e.g., In re Garnero, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1969) (recitation of "interbonded one to another by interfusion between the surfaces of the perlite particles" construed as structural limitation in product claim); In re Dike, 394 F.2d 584, 589, 157 USPQ 581, 585 (CCPA 1968)

(no error in USPTO board holding that term "blowmolded" in claims drawn to integral plastic container and handle failed to distinguish over prior art, because term related to process of making the article, and was not definitive as to the structure of the article). Here, the process step "chemically modified so that they are free of said particular amino acid" does not add a structural limitation to the "array of polypeptide capture agents" because the resulting product is "an array of polypeptide capture agents" that are free of a particular amino acid regardless how the amino acid is excluded from the capture agents. Thus, this process limitation does not impart patentability to the claimed array in accordance with In re Dike.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1639
1/13/2007

JON EPPERSON
PRIMARY EXAMINER